

## WEST Search History

DATE: Sunday, July 28, 2002

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB; PLUR=YES; OP=ADJ</i>			
L11	L10 and @pd<20000419	105	L11
L10	l9 and l6	250	L10
L9	ligand and l8 and l7	600	L9
L8	protein or polypeptide	139662	L8
L7	nuclear receptor	808	L7
L6	l5 or l4 or l3 or l2 or l1	23908	L6
L5	((530/399)!.CCLS.) )	1244	L5
L4	((530/350)!.CCLS.) )	7184	L4
L3	((536/23.1)!.CCLS.) )	7087	L3
L2	((435/7.1)!.CCLS.) )	4360	L2
L1	((435/6)!.CCLS.) )	10913	L1

END OF SEARCH HISTORY

=> d his

(FILE 'HOME' ENTERED AT 14:12:51 ON 28 JUL 2002)

FILE 'HCAPLUS' ENTERED AT 14:13:21 ON 28 JUL 2002

L1	5446 S NUCLEAR RECEPTOR
L2	11362 S REGULATORY PROTEIN
L3	38 S L1 (L) L2
L4	655 S LIBRA? (W) (NUCLEIC ACID OR NUCLEOTIDE OR POLYNUCLEOTIDE)
L5	0 S L3 AND L4
L6	26 S L3 AND PD<19990419

=> d ibib ab 1-26

L6 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:92454 HCAPLUS

DOCUMENT NUMBER: 133:1776

TITLE: Initial characterization of new orphan receptors

AUTHOR(S): Sladek, R.; Giguere, V.

CORPORATE SOURCE: Molecular Oncology Group, McGill University Health Centre, Montreal, H3A 1A1, Can.

SOURCE: Nuclear Receptors (1999), 29-69. Editor(s): Picard, Didier. Oxford University Press: Oxford, UK. CODEN: 68QAA8

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review with 41 refs. **Nuclear receptors** are transcription factors with the intrinsic ability to be regulated by changes in the intracellular levels of small lipophilic compds. Since the mol. cloning of the glucocorticoid receptor in 1985, over 50 members of the **nuclear receptor** superfamily have been identified. Most of these gene products were discovered as a result of their sequence homol. with other family members; however, their sequence conservation often reveals little about their individual function as transcription **regulatory proteins**. The ultimate goal for many investigators is to identify ligands for these orphan receptors: basic characterization of receptor functions including their DNA binding mode and transactivation properties provides an important first step toward realizing this goal. The identification of synthetic and natural response elements is a crit. first step toward identifying potential in vivo roles for newly discovered members of the **nuclear receptor** family. While this approach relies heavily on in vitro studies, its success has been well demonstrated by promoter characterization expts., which have identified a wide spectrum of genes which may be regulated by classical steroid and thyroid hormones as well as by retinoids and synthetic agents such as peroxisome proliferators. Here, exptl. protocols used to define the DNA binding, dimerization, and transcriptional properties of a novel orphan **nuclear receptor** are described.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:46176 HCAPLUS

DOCUMENT NUMBER: 132:203682

TITLE: Nuclear receptors: coactivators, corepressors and chromatin remodeling in the control of transcription

AUTHOR(S): Collingwood, T. N.; Urnov, F. D.; Wolffe, A. P.

CORPORATE SOURCE: Laboratory of Molecular Embryology, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892-5431, USA

SOURCE: Journal of Molecular Endocrinology (1999), 23(3), 255-275

CODEN: JMLEEI; ISSN: 0952-5041

PUBLISHER: Society for Endocrinology

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with .apprx.175 refs. A contemporary view of hormone action at the transcriptional level requires knowledge of the transcription factors including the hormone receptor that may bind to promoters or enhancers, together with the chromosomal context within which these **regulatory proteins** function. **Nuclear receptors** provide the best examples of transcriptional control through the targeted recruitment of large protein complexes that modify chromosomal components and reversibly stabilize or destabilize chromatin. Ligand-dependent recruitment of transcriptional coactivators destabilizes chromatin by mechanisms including histone acetylation and contacts with the basal transcriptional machinery. In contrast, the recruitment of corepressors in the absence of ligand or in the presence of hormone

antagonists serves to stabilize chromatin by the targeting of histone deacetylases. Both activation and repression require the action of other chromatin remodeling engines of the switch 2/sucrose nonfermentable 2 (SWI2/SNF2) class. Here the authors summarize this information and integrate hormone action into a chromatin context.

REFERENCE COUNT: 174 THERE ARE 174 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:219069 HCAPLUS

DOCUMENT NUMBER: 131:15834

TITLE: Visualizing protein-protein interactions in the nucleus of the living cell

AUTHOR(S): Day, Richard N.; Nordeen, Steven K.; Wan, Yihong

CORPORATE SOURCE: Departments of Medicine and Cell Biology, National Science Foundation Center for Biological Timing, University of Virginia Health Sciences Center, Charlottesville, VA, 22908, USA

SOURCE: Molecular Endocrinology (1999), 13(4), 517-526

CODEN: MOENEN; ISSN: 0888-8809

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 63 refs. In this paper we review the characteristics of the GFPs that make them useful for the study of nuclear protein behavior in living cells. For many important physiol. processes such as the regulation of transcription by the **nuclear receptors** and their coregulatory partners the crit. events are coordinated in space and time through sequential but transient interactions within complex macromol. assemblies. The power of the fluorescence resonance energy transfer (FRET) approach is in the detection of these intricate social behaviors between **regulatory proteins** in their natural environment within the living cell.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:814234 HCAPLUS

DOCUMENT NUMBER: 130:205818

TITLE: Binding specificity and modulation of the human ApoCIII promoter activity by heterodimers of ligand-dependent nuclear receptors

AUTHOR(S): Lavrentiadou, Sophia N.; Hadzopoulou-Cladaras, Margarita; Kardassis, Dimitris; Zannis, Vassilis I.

CORPORATE SOURCE: Departments of Medicine and Biochemistry Cardiovascular Institute Section of Molecular Genetics, Boston University Medical Center, Boston, MA, 02118, USA

SOURCE: Biochemistry (1999), 38(3), 964-975

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human apolipoprotein CIII (apoCIII) is a major determinant of plasma triglyceride metab. The regulatory elements that control both hepatic and intestinal transcription of the human apoCIII gene are localized between nucleotides -792 and -25 of the apoCIII promoter. Elements important for apoCIII promoter activity are three hormone response elements (HREs) and three SP1-binding sites. Orphan members of the nuclear hormone receptor superfamily can bind the HREs and strongly enhance or repress apoCIII promoter activity. In the present study we have investigated the ability of ligand-dependent nuclear hormone receptors to bind and modulate the human apoCIII promoter activity. Expts. using DNA binding and competition assays showed that the proximal element B (-87/-72) binds strongly, in addn. to HNF-4, ARP-1, EAR-2, and EAR-3, heterodimers of RXR.alpha. with

RAR.alpha., and less efficiently, homodimers of RAR.alpha. and heterodimers of RXR.alpha. with T3R.beta. or PPAR.alpha.. Element G (-669/-648), which was shown previously to bind ARP-1 and EAR-3 but not HNF-4, binds strongly heterodimers of RXR.alpha. with either RAR.alpha. or T3R.beta.. Finally element I4 (-732/-712), which was shown to bind HNF-4, also binds strongly ARP-1 and EAR-3, as well as RXR.alpha./RAR.alpha. heterodimers and less efficiently, RXR.alpha./T3R.beta. heterodimers. Methylation interference expts. have identified the protein-DNA interactions between different nuclear receptors and the resp. HREs on the apoCIII promoter. RXR.alpha./RAR.alpha. heterodimers and HNF-4 homodimers bind to DR-1 motifs on elements B and I4, resp. RXR.alpha./T3R.beta. heterodimers and ARP-1 bind to DR-5 and DR-0 motifs resp. on element G. Cotransfection expts. in HepG2 cells showed that RXR.alpha. or a combination of RXR.alpha. and RAR.alpha. increased the apoCIII promoter activity approx. 2-fold in the presence of the ligands 9-cis or all-trans RA. In contrast, a combination of RXR.alpha. and T3R.beta. transactivated the apoCIII promoter 1.5-fold in the presence of 9-cis RA but it repressed the apoCIII promoter activity in the presence of T3. Mutations in the HREs of elements B, G, or I4 or in the SP1-binding site of element H, which abolished the binding of nuclear hormone receptors or SP1 to their cognate site, reduced the promoter strength and exhibited different responses to the ligand-dependent nuclear receptors. The findings suggest that modulation of the apoCIII promoter activity by orphan and ligand-dependent nuclear receptors involves complex interactions among nuclear receptors, SP1 and possibly other factors bound to the enhancer and the proximal promoter region.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:763254 HCAPLUS

DOCUMENT NUMBER: 130:120384

TITLE: A winged-helix family member is involved in a steroid hormone-triggered regulatory circuit

AUTHOR(S): Dean, Diane M.; Berger, Ryan R.; Sanders, Michel M.

CORPORATE SOURCE: Department of Biochemistry, Molecular Biology, and Biophysics, University of Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Endocrinology (1998), 139(12), 4967-4975

CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A common theme emerging in eukaryotic gene regulation is that maximal gene induction requires several transcription factors acting in concert to regulate the activation of crit. genes. Increasingly, **nuclear receptors** play key roles in orchestrating this regulation, often by integrating addnl. signaling pathways, through complex regulatory elements known as hormone response units. The ovalbumin gene contains one such unit, known as the steroid-dependent regulatory element. The binding of the chicken ovalbumin induced **regulatory protein-I** (Chirp-I) to this element occurs only in response to treatment with estrogen and glucocorticoid. Evidence presented herein demonstrates that Chirp-I has many features in common with the winged-helix (W-H) family of transcription factors. The binding sites for Chirp-I and for the W-H proteins have similar sequence recognition requirements. Northern blots establish that members of the W-H family are expressed in oviduct. Most convincing, the Chirp-I complex interacts with two different antibodies specific to W-H family members. The culmination of this work supports the hypothesis that Chirp-I is a member of the W-H family, and it lends credence to the idea that W-H proteins are essential components of some steroid hormone regulatory circuits.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:486883 HCAPLUS

DOCUMENT NUMBER: 129:199380  
TITLE: TIF1.alpha.: a possible link between KRAB zinc finger proteins and nuclear receptors  
AUTHOR(S): Le Douarin, B.; You, J.; Nielsen, A. L.; Chambon, P.; Losson, R.  
CORPORATE SOURCE: Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/ULP, College de France, Illkirch, 67404, Fr.  
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1998), 65(1-6), 43-50  
CODEN: JSBBEZ; ISSN: 0960-0760  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review with 35 refs. Ligand-induced gene activation by **nuclear receptors** (NRs) is thought to be mediated by transcriptional intermediary factors (TIFs), that interact with their ligand-dependent activation function AF-2 activating domain. Included in the group of the putative AF-2 TIFs identified so far is TIF1.alpha., a member of a new family of proteins which contains an N-terminal RBCC (RING finger-B boxes-coiled coil) motif and a C-terminal bromodomain preceded by a PHD finger (C4HC3 zinc-finger motif). In addn. to these conserved domains present in a no. of transcriptional **regulatory proteins**, TIF1.alpha. contains several protein-protein interaction sites. Of these, one specifically interacts with NRs bound to their agonistic ligand and not with NR mutants that are defective in the AF-2 activity. Immediately adjacent to this "NR box", TIF1.alpha. contains an interaction site for members of the chromatin organization modifier (chromo) family, HP1.alpha. and MOD1, which both are heterochromatinic proteins. Finally, TIF1.alpha. also has a binding site for KRAB silencing domains of C2H2 zinc finger proteins. TIF1.beta., another member of the TIF1 gene family, has some interacting partners in common with TIF1.alpha.. TIF1.beta. can interact with HP1.alpha., MOD1, and KRAB domains, but apparently not with NRs. Both TIF1.alpha. and TIF1.beta. repress transcription when fused to a DNA binding domain in transiently transfected mammalian cells. A model discussing the potential function(s) of TIF1s in the control of transcription at the level of the chromatin template is presented.

L6 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:391572 HCAPLUS  
DOCUMENT NUMBER: 129:118699  
TITLE: Multiple parameters determine the specificity of transcriptional response by nuclear receptors HNF-4, ARP-1, PPAR, RAR and RXR through common response elements  
AUTHOR(S): Nakshatri, Harikrishna; Bhat-Nakshatri, Poornima  
CORPORATE SOURCE: Department of Surgery, Indiana University School of Medicine, Indianapolis, IN, 46202, USA  
SOURCE: Nucleic Acids Research (1998), 26(10), 2491-2499  
CODEN: NARHAD; ISSN: 0305-1048  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A no. of **nuclear receptors**, including retinoic acid receptors (RARs), retinoid-X receptors (RXRs), hepatocyte nuclear factor 4 (HNF-4), chicken ovalbumin upstream promoter transcription factor I (COUP-TFI), apolipoprotein **regulatory protein 1** (ARP-1) and peroxisome proliferator-activated receptor (PPAR), bind to response elements comprised of two core motifs, 5'-RG(G/T)TCA, or a closely related sequence sepd. by 1 nt (DR1 elements). The potential role of the precise sequence of the core motif as well as the spacer nucleotide in detg. specificity and promiscuity of receptor-response element interactions was investigated. We show here that nucleotides at base positions 1, 2 and 4 of the core motif as well as the spacer nucleotide det. the binding preference of HNF-4 and ARP-1 homodimers and RAR:RXR and PPAR:RXR heterodimers. In transfection expts. transcriptional activation

by HNF-4 and PPAR:RXR and repression by ARP-1 correlated with the relative in vitro binding affinity provided the element was located within the proper promoter context. Furthermore, promoter context also detd. whether an element that binds to HNF-4 and PPAR:RXR with equal affinity functions as an HNF-4 response element or PPAR response element. Thus, apart from the element-specific differences in affinity for the receptors, addnl. promoter-specific transcription factors that interact with HNF-4 and PPAR:RXR det. the specificity of transcriptional response through DR1-type elements.

L6 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:369361 HCAPLUS

DOCUMENT NUMBER: 129:107312

TITLE: Histone deacetylase associated with mSin3A mediates repression by the acute promyelocytic leukemia-associated PLZF protein

AUTHOR(S): David, Gregory; Alland, Leila; Hong, Suk-Hyun; Wong, Chi-Wai; Depinho, Ronald A.; Dejean, Anne

CORPORATE SOURCE: Unite de Recombinaison et Expression Genetique, INSERM U163, Institut Pasteur, Paris, 75724, Fr.

SOURCE: Oncogene (1998), 16(19), 2549-2556

CODEN: ONCNES; ISSN: 0950-9232

PUBLISHER: Stockton Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The PLZF gene was identified first by its fusion with the retinoic acid receptor .alpha. gene in the t(11;17) translocation assocd. with a retinoic acid resistant form of acute promyelocytic leukemia (APL). It encodes a Kruppel-like zinc finger protein with a POZ domain shared with a subset of **regulatory proteins** including the BCL6 leukemogenic protein. PLZF, like BCL6, strongly represses transcription initiated from different promoters. Here the authors show that PLZF assoc. in vitro and in vivo with the Mad co-repressor mSin3A and the histone deacetylase HDAC1. Two domains in PLZF and the PAH1 structure of mSin3A mediate these interactions. Trichostatin A, a specific inhibitor of histone deacetylases, significantly reduces PLZF repression. These data strongly suggest that, like **nuclear receptors** and Mad, PLZF represses transcription by recruiting a histone deacetylase through the SMRT-mSin3-HDAC co-repressor complex. The authors also show that BCL6 assoc. with HDAC1 indicating that this type of regulation might be common to POZ/Zinc finger proteins involved in human leukemias. This work supports a role for deregulated histone deacetylation in the development of both lymphoid and myeloid neoplasia in human and suggests that targeted histone deacetylase inhibitors may be useful for treatment of certain types of malignancies.

L6 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:350717 HCAPLUS

DOCUMENT NUMBER: 129:77008

TITLE: 25-Hydroxycholesterol is not a ligand for the orphan nuclear receptor steroidogenic factor-1 (SF-1)

AUTHOR(S): Mellon, Synthia H.; Bair, Susanna R.

CORPORATE SOURCE: Department of Obstetrics, Gynecology and Reproductive Sciences, The Reproductive Endocrinology Center, University of California, San Francisco, 94143-0556, USA

SOURCE: Endocrinology (1998), 139(6), 3026-3029

CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The orphan **nuclear receptor** steroidogenic factor-1 (SF-1) is involved in the transcriptional regulation of all the steroid hydroxylase genes, and also regulates the transcription of the genes for Mullerian Inhibitory substance (MIS), alpha subunit of glycoprotein hormone, LH.beta., oxytocin, GnRH receptor, ACTH receptor, prolactin receptor, DAX-1, and steroidogenic acute **regulatory**

**protein.** Other members of the **nuclear receptor** gene family, including steroid hormone, thyroid hormone, retinoic acid, PPAR, and vitamin D receptors must bind ligand to activate transcription, but SF-1 has been considered to be an orphan **nuclear receptor** because, when identified, it had no known ligand. A recent publication suggested that transcriptional regulation by SF-1, expressed in a non-steroidogenic CV-1 cells, could be activated by oxysterols suggesting that these compds. could serve as natural ligands for SF-1. The authors now demonstrate that 25-hydroxycholesterol, either added exogenously or synthesized endogenously in steroidogenic mouse Leydig MA-10 cells, did not act as a ligand for SF-1, as it did not increase transcription from six different SF-1-dependent DNA sequences. Furthermore, the abundance of these oxysterols in MA-10 cells was much less than concns. needed for activation of SF-1 in CV-1 cells, indicating that SF-1 is not constitutively bound by ligand in MA-10 cells. Thus, in steroidogenic cells, transcriptional regulation of the steroid hydroxylase genes by SF-1 does not depend upon the presence of 25-hydroxycholesterol, and is not modified by its presence.

L6 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:237375 HCAPLUS

DOCUMENT NUMBER: 129:63914

TITLE: The CYP2B2 phenobarbital response unit contains an accessory factor element and a putative glucocorticoid response element essential for conferring maximal phenobarbital responsiveness

AUTHOR(S): Stoltz, Catherine; Vachon, Marie-Helene; Trottier, Eric; Dubois, Stephane; Paquet, Yanick; Anderson, Alan  
CORPORATE SOURCE: Cent. Recherche Cancerol. Univ. Laval, Cent. Hosp., Univ. Quebec, Quebec, G1R 2J6, Can.

SOURCE: Journal of Biological Chemistry (1998), 273(14), 8528-8536

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hepatic cytochrome P450s play a crit. role in the metab. of hydrophobic xenobiotics. One of the major unsolved problems in xenobiotic metab. is the mol. mechanism whereby phenobarbital induces hepatic enzymes, particularly CYP2B1 and CYP2B2 in rat liver. By using primary rat hepatocytes for transfection analyses, we previously identified in the CYP2B2 5'-flank a 163-base pair Sau3AI fragment that confers phenobarbital inducibility on a cat reporter gene and that has the properties of a transcriptional enhancer. Transfection expts. with sub-regions of the Sau3AI fragment now indicate that a central core together with an upstream or downstream accessory element within the fragment can confer phenobarbital responsiveness. One such accessory element, AF1, was identified and localized. DNase I footprinting anal. revealed the presence of a footprint overlapping this AF1 element. It also identified three other major protected regions, two of which are putative recognition sites for known transcription factors. Site-directed mutagenesis indicated that a putative glucocorticoid response element as well as a nuclear factor 1 site and an assocd. **nuclear receptor** hexamer half-site are essential for conferring maximal phenobarbital inducibility. Taken together, the results indicate that phenobarbital induction of CYP2B2 requires interactions among multiple **regulatory proteins** and cis-acting elements constituting a phenobarbital response unit.

L6 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:39561 HCAPLUS

DOCUMENT NUMBER: 128:176859

TITLE: A binding site for nuclear receptors is required for the differential expression of the aldolase A fast-twitch muscle promoter in body and head muscles  
AUTHOR(S): Spitz, Francois; Demignon, Josiane; Demeurie,



Jeannine; Sabourin, Jean-Christophe; Kahn, Axel;  
Daegelen, Dominique; Maire, Pascal  
CORPORATE SOURCE: INSERM U129, ICGM, Universite Rene Descartes Paris V,  
Paris, 19104, Fr.  
SOURCE: Journal of Biological Chemistry (1998),  
273(1), 561-567  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular  
Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB In hind limb muscles, the aldolase A muscle-specific promoter is specifically expressed in glycolytic fast-twitch fibers. Here, we show that in addn., it is expressed at higher levels in trunk and limb muscles than in neck and head muscles independent of their fiber-type content. We have identified by anal. of transgenic mice a DNA element that is required for this differential expression. and, to a lesser extent, for fiber-type specificity. We show that members of the nuclear receptor superfamily bind this element in skeletal muscle nuclear exts. Interestingly, in gel mobility shift assays, different complexes were formed with this sequence in tongue nuclear exts. compared with limb or trunk muscle nuclear exts. Therefore, binding of distinct nuclear receptors to a single regulatory sequence appears to be assocd. with the location-dependent expression of the aldolase A muscle-specific promoter.

L6 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:747820 HCAPLUS  
DOCUMENT NUMBER: 128:71541  
TITLE: DNA binding and transcriptional repression by DAX-1  
blocks steroidogenesis  
AUTHOR(S): Zazopoulos, Emmanuel; Lalli, Enzo; Stocco, Douglas M.;  
Sassone-Corsi, Paolo  
CORPORATE SOURCE: Inst. Genetique et de Biologie Moleculaire et  
Cellulaire, CNRS-INSERM-ULP BP 163, Strasbourg, 67404,  
Fr.  
SOURCE: Nature (London) (1997), 390(6657), 311-315  
CODEN: NATUAS; ISSN: 0028-0836  
PUBLISHER: Macmillan Magazines  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Mutations in the DAX-1 gene are responsible for congenital X-linked adrenal hypoplasia, a disease that is assocd. with hypogonadotropic hypogonadism. DAX-1 expression is tissue-specific and is finely regulated throughout development, suggesting that it has a role in both adrenal and gonadal function. DAX-1 is an unusual member of the **nuclear-receptor** superfamily of transcription factors which contains no canonical zinc-finger or any other known DNA-binding motif. Binding sites for DAX-1 are found in the promoters of the dax-1 and StAR (for steroidogenic acute **regulatory protein**) genes. Here we show that DAX-1 binds DNA and acts as a powerful transcriptional repressor of StAR gene expression, leading to a drastic decrease in steroid prodn. We provide in vitro and in vivo evidence that DAX-1 binds to DNA hairpin structures. Our results establish DAX-1 as the first member of the **nuclear receptor** superfamily with novel DNA-binding features and reveal that it has regulatory properties crit. to the understanding of its physiol. functions.

L6 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:116698 HCAPLUS  
DOCUMENT NUMBER: 126:185389  
TITLE: Retinoic acid increases cellular retinol binding  
protein II mRNA and retinol uptake in the human  
intestinal Caco-2 cell line  
AUTHOR(S): Levin, Marc S.; Davis, Alan E.  
CORPORATE SOURCE: Dep. Med., Washington Univ. Sch. Med., St. Louis, MO,  
63110, USA  
SOURCE: Journal of Nutrition (1997), 127(1), 13-17

PUBLISHER: American Society for Nutritional Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Cellular retinol binding protein II (CRBP<sub>II</sub>) is an abundant small intestinal protein that facilitates vitamin A trafficking and metab. The magnitude of retinol uptake and metab. correlate to CRBP<sub>II</sub> levels in the human intestinal Caco-2 cell line. To investigate the importance of retinoic acid receptor response elements in the promoter of the CRBP<sub>II</sub> gene, retinoic acid regulation of CRBP<sub>II</sub> expression and vitamin A absorption was studied in differentiated Caco-2 cells. All-trans- or 9-cis-retinoic acid increased CRBP<sub>II</sub> mRNA levels 2-3-fold. This was assocd. with a 50% increase in retinol absorption. Retinoic acid receptor .beta. and apolipoprotein A1 **regulatory protein-1**, two **nuclear receptors** that bind to the CRBP<sub>II</sub> promoter, were also induced, whereas other retinoid and orphan receptors were not. Thus, retinoic acid may regulate CRBP<sub>II</sub> expression directly or by selectively changing levels of **nuclear receptors** or other factors. These studies are the first to demonstrate that retinoic acid can modulate endogenous CRBP<sub>II</sub> mRNA levels and retinol absorption in Caco-2 cells and suggest that human intestinal vitamin A absorption may be regulated by retinoids.

L6 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:108654 HCAPLUS

TITLE: Regulation of expression of the steroidogenic acute regulatory protein (StAR) gene: a central role for steroidogenic factor 1

AUTHOR(S): Sugawara, Teruo; Kiriakidou, Marianthi; Mcallister, Jan M.; Holt, John A.; Arakane, Futoshi; Strauss, Jerome F., III

CORPORATE SOURCE: Center for Research on Reproduction and Women's Health, University of Pennsylvania Medical Center, Philadelphia, PA, 19104, USA

SOURCE: Steroids (1997), 62(1), 3-4  
CODEN: STEDAM; ISSN: 0039-128X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; Miscellaneous

LANGUAGE: English

AB Steroidogenic acute **regulatory protein** (StAR) plays a crit. role in regulating the rate-limiting step in steroid hormone synthesis, cholesterol side-chain cleavage. StAR gene expression is transcriptionally controlled in the gonads by gonadotropic hormones via a cAMP second message. We have begun to analyze factors responsible for the transcriptional activation of the StAR gene. The human StAR gene promoter has at least two cis elements that govern basal and cAMP-regulated gene expression. One of these elements (the distal element) is a consensus binding sequence for the orphan **nuclear receptor** transcription factor, steroidogenic factor 1 (SF-1); the other (the proximal element) is a related motif. The human StAR promoter is not active in BeWo choriocarcinoma cells, but is functional and cAMP-responsive in murine Y1 adrenal cortical tumor cells. Cotransfection of a plasmid expressing SF-1 allows a StAR promoter construct to function in BeWo cells. Other orphan nuclear transcription factors do not support StAR promoter function in BeWo cell hosts. Deletion or mutation of the distal and proximal cis elements individually substantially reduces SF-1-supported StAR promoter activity. The distal site binds SF-1 with high affinity, whereas the proximal site binds SF-1 with lower affinities. These findings demonstrate a requirement for SF-1 for human StAR gene expression.

L6 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:94530 HCAPLUS

DOCUMENT NUMBER: 126:208104

TITLE: Characterization of the promoter region of the mouse gene encoding the steroidogenic acute regulatory protein

AUTHOR(S): Caron, Kathleen M.; Ikeda, Yayoi; Soo, Shiu-Ching;  
Stocco, Douglas M.; Parker, Keith L.; Clark, Barbara  
J.  
CORPORATE SOURCE: Medical Center, Duke University, Durham, NC, 27710,  
USA  
SOURCE: Molecular Endocrinology (1997), 11(2),  
138-147  
CODEN: MOENEN; ISSN: 0888-8809  
PUBLISHER: Endocrine Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Steroidogenic acute **regulatory protein** (StAR) delivers  
cholesterol to the inner mitochondrial membrane, where the cholesterol  
side-chain cleavage enzyme carries out the first committed step in steroid  
hormone biosynthesis. StAR expression is restricted to steroidogenic  
cells and is rapidly induced by treatment with trophic hormones or cAMP.  
We analyzed the 5'-flanking region of the mouse StAR gene to elucidate the  
mechanisms that regulate its cell-specific and hormone-induced expression.  
In transient transfection assays, a luciferase reporter gene driven by the  
StAR 5'-flanking region was preferentially expressed by steroidogenic Y1  
adrenocortical and MA-10 Leydig cells in a cAMP-responsive manner.  
5'-Deletion and site-directed mutagenesis studies identified a region  
between -254 and -113 that is essential for full levels of promoter  
activity. This region contains a binding site for the orphan  
**nuclear receptor** steroidogenic factor-1 (SF-1) that,  
although not required for hormone induction, is crit. for basal promoter  
activity, thus implicating SF-1 in StAR expression. Analyses of knockout  
mice deficient in SF-1 further supported an important role for SF-1 in  
StAR gene expression. These studies provide novel insights into the  
mechanisms that regulate StAR gene expression and extend our understanding  
to SF-1's global roles within steroidogenic cells.

L6 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:403630 HCAPLUS  
DOCUMENT NUMBER: 125:82526  
TITLE: Molecular basis of skeletal muscle regeneration  
AUTHOR(S): Chambers, Rebecca L.; McDermott, John C.  
CORPORATE SOURCE: Faculty of Pure and Applied Science, York University,  
Toronto, ON, M3J 1P3, Can.  
SOURCE: Can. J. Appl. Physiol. (1996), 21(3),  
155-184  
CODEN: CJAPEY; ISSN: 1066-7814  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review with 133 refs. Skeletal muscle regeneration is a vital process  
with important implications for various muscle myopathies and adaptations  
to physiol. overload. Few of the mol. **regulatory**  
**proteins** controlling this process have so far been identified.  
Several growth factors have defined effects on myogenic precursor cells  
and appear to also be involved during regeneration. In addn., factors  
that may be released by cells of the immune system may activate satellite  
cells during regeneration. Many of these growth factors are assocd. with  
signaling cascades which transmit information to the nucleus. The  
**nuclear "receptors"** that receive the incoming signals  
are transcription factors that interact with DNA regulatory sequences to  
modulate gene expression. Of the nuclear factors isolated so far, the  
immediate-early genes are assocd. with muscle precursor cell  
proliferation. This review aims to synthesize the extensive research on  
myogenic differentiation and relate this to research concerning the mol.  
regulation of skeletal muscle regeneration.

L6 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:377384 HCAPLUS  
DOCUMENT NUMBER: 125:50644  
TITLE: Steroidogenic factor 1-dependent promoter activity of  
the human steroidogenic acute regulatory protein  
(StAR) gene

AUTHOR(S): Sugawara, Teruo; Holt, John A.; Kiriakidou, Marianthi;  
Strauss, Jerome F., III  
CORPORATE SOURCE: School of Medicine, University of Pennsylvania,  
Philadelphia, PA, 19104, USA  
SOURCE: Biochemistry (1996), 35(28), 9052-9059  
CODEN: BICHAW; ISSN: 0006-2960  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Steroidogenic acute **regulatory protein** (StAR) is required for efficient adrenal cortical and gonadal but not trophoblast steroid hormone synthesis. StAR gene expression in gonadal cells is stimulated by tropic hormones acting through the intermediacy of cAMP. DNA sequence anal. of the human StAR gene promoter revealed 2 motifs resembling binding sites for steroidogenic factor 1 (SF-1), a member of the orphan **nuclear receptor** transcription factor family that controls expression of steroidogenic hydroxylases. The 5'-most sequence (distal site) is a consensus SF-1 binding site. The proximal site is a consensus estrogen receptor binding half-site. The StAR gene promoter is not active in BeWo choriocarcinoma cells, COS-1 cells, HeLa cells, or SK-OV-3 ovarian adenocarcinoma cells, all of which do not express significant levels of SF-1 mRNA. Introduction of SF-1 into these cells stimulated StAR promoter activity, particularly in response to cAMP. Two orphan nuclear transcription factors that bind to sequences similar to SF-1 sites, NGFI-B/Nur77 and RNR-1, did not support cAMP-stimulated StAR promoter activity in BeWo cells. Mutation of the distal putative SF-1 binding site reduced basal and cAMP-stimulated promoter activity in BeWo cells by 82% and 71%, resp. Mutation of the proximal putative SF-1 binding site reduced basal and cAMP-stimulated promoter activity by 89% and 96%, resp. Mutations in both sites reduced basal promoter activity to 7% of wild type promoter activity and cAMP-stimulated promoter activity to <5% of the wild type. Deletion analyses of promoter activity were consistent with the mutation studies. Electrophoretic mobility shift assays (EMSAs) demonstrated that the distal site binds to SF-1 expressed in COS-1 cells and to an SF-1-GST fusion protein with high affinity, but that the mutated distal sequence does not. An anti-SF-1 antibody ablated the characteristic SF-1-DNA complex with the distal sequence. The proximal site formed a no. of protein-DNA complexes with COS-1 cell exts., but appeared to have at best only very modest affinity for SF-1. Collectively, these findings demonstrate that SF-1 plays a key role in controlling the basal and cAMP-stimulated expression of the StAR gene. SF-1 can function at 2 distinct sites in the human StAR gene promoter, apparently by 2 different types of interaction, to control transcription.

L6 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:917394 HCAPLUS

DOCUMENT NUMBER: 123:306706

TITLE: The role of nuclear hormone receptors in mammalian development

AUTHOR(S): Parker, Keith L.; Schimmer, Bernard P.

CORPORATE SOURCE: Duke University Medical Center, Durham, NC, USA

SOURCE: Curr. Opin. Endocrinol. Diabetes (1995),  
2(5), 392-7

CODEN: CENDES; ISSN: 1068-3097

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 31 refs. The nuclear hormone receptor family is a group of transcriptional **regulatory proteins** that mediates the actions of diverse ligands, including steroid hormones, thyroid hormone, vitamin D, and retinoids. During the past year, gene knockout technol. has been used to selectively ablate both ligand-activated and orphan **nuclear receptors** in mice, with exciting and sometimes unexpected results. Other reports describe natural mutations of receptor family members in patients with specific developmental abnormalities.

L6 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:584908 HCAPLUS  
DOCUMENT NUMBER: 123:220190  
TITLE: The N-terminal part of TIF1, a putative mediator of the ligand-dependent activation function (AF-2) of nuclear receptors, is fused to B-raf in the oncogenic protein T18  
AUTHOR(S): Le Douarin, Bertrand; Zechel, Christina; Garnier, Jean-Marie; Lutz, Yves; Tora, Laszlo; Pierrat, Benoit; Heery, David; Gronemeyer, Hinrich; Chambon, Pierre; Losson, Regine  
CORPORATE SOURCE: Inst. de Genetique et de Biologie Moleculaire et Cellulaire, College de France, Strasbourg, 67404, Fr.  
SOURCE: EMBO J. (1995), 14(9), 2020-33  
CODEN: EMJODG; ISSN: 0261-4189  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB **Nuclear receptors** (NRs) bound to response elements mediate the effects of cognate ligands on gene expression. Their ligand-dependent activation function, AF-2, presumably acts on the basal transcription machinery through intermediary proteins/mediators. We have isolated a mouse nuclear protein, TIF1, which enhances RXR and RAR AF-2 in yeast and interacts in a ligand-dependent manner with several NRs in yeast and mammalian cells, as well as in vitro. Remarkably, these interactions require the amino acids constituting the AF-2 activating domain conserved in all active NRs. Moreover, the estrogen receptor (ER) AF-2 antagonist hydroxytamoxifen cannot promote ER-TIF1 interaction. We propose that TIF1, which contains several conserved domains found in transcriptional **regulatory proteins**, is a mediator of ligand-dependent AF-2. Interestingly, the TIF1 N-terminal moiety is fused to B-raf in the mouse oncoprotein T18.

L6 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:468165 HCAPLUS  
DOCUMENT NUMBER: 122:283755  
TITLE: Involvement of early growth response factor Egr-1 in apolipoprotein AI gene transcription  
AUTHOR(S): Kilbourne, Edward J.; Widom, Russell; Harnish, Douglas C.; Malik, Sohail; Karathanasis, Sotirios K.  
CORPORATE SOURCE: Dep. Cardiovascular Molecular Biol., Lederle Lab., Pearl River, NY, 10965, USA  
SOURCE: J. Biol. Chem. (1995), 270(12), 7004-10  
CODEN: JBCHA3; ISSN: 0021-9258  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Liver-specific expression of the apolipoprotein AI (apoAI) gene is mediated by transcription factors bound to 3 sites (A, B, and C) in the apoAI enhancer. Sites A and C bind various members of the **nuclear receptor** superfamily, including the orphan **nuclear receptor** apolipoprotein **regulatory protein-1** (ARP-1); site B binds the liver-enriched factor hepatic nuclear factor-3. The immediate early growth response factor (Egr-1), which is transiently expressed in various pathophysiol. states of the liver, activates the apoAI enhancer and overcomes ARP-1-mediated repression of the enhancer in hepatoblastoma HepG2 cells. Deletion mapping anal. revealed two Egr-1 binding sites, E1 and E2, flanking site A. Egr-1 bound efficiently to both E1 and E2. Sp1 in HepG2 nuclear exts. bound to E2 but not E1. In HepG2 cells, E1 functioned as an Egr-1 response element, whereas E2 had high basal activity and was not further induced by Egr-1. Mutations that prevent Egr-1 binding to the apoAI enhancer abolished its responsiveness to Egr-1, whereas they had only minor effects on its constitutive activity. These mutations also diminished the ability of Egr-1 to overcome ARP-1-mediated repression. Elimination of transcription factor binding to sites A, B, or C reduced enhancer activity without affecting Egr-1-dependent activation. It is proposed that Egr-1 is recruited to the apoAI enhancer complex under unusual circumstances, such as those prevailing during liver regeneration, to maintain apoAI transcription levels by overriding prior transcriptional controls.

L6 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:357742 HCAPLUS  
DOCUMENT NUMBER: 122:283724  
TITLE: Characterization of orphan receptor DNA-binding enhancer  
AUTHOR(S): Rhee, Myungchull  
CORPORATE SOURCE: Howard Hughes Med. Inst., Brigham Women's Hosp.  
Harvard Med. Sch., Boston, MA, 02115, USA  
SOURCE: Molecules and Cells (1994), 4(4), 457-62  
CODEN: MOCEEK; ISSN: 1016-8478  
PUBLISHER: Korean Society of Molecular Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Apolipoprotein AI **regulatory protein-1** (ARP-1) binds to a regulatory element which is composed of two direct repeat motifs (site A), TGAACCCT and TGACCCCT in the apolipoprotein AI (apo AI) gene as a dimer. Because the ligand of ARP-1 has not been identified, ARP-1 is classified as an orphan receptor. ARP-1 binds to various hormone response elements as a homodimer and/or a heterodimer. In most cases, they antagonize the transcriptional stimulation exerted by various **nuclear receptors** and their corresponding ligands. To better understand the mol. mechanism wherein ARP-1 functions as a transcriptional repressor, COS-1 cellular ext. was analyzed for its effect on the DNA binding capacity of ARP-1. First, this report showed that a heat-stable protein (complex), designated orphan receptor DNA-binding enhancer (ORDE), enhanced orphan receptors', such as ARP-1, chicken ovalbumin upstream promoter transcriptional factor (COUP-TF), and hepatocyte nuclear factor 4 (HNF4) binding to site A. Second, ORDE changed the DNA binding capacity, but neither the affinity nor the location of the band in EMSA, of ARP-1. Finally, ORDE interacted with the DNA binding domain of ARP-1. Taken together, these results suggest that a battery of orphan receptors may require ORDE to bind their cognate DNA sequences.

L6 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:236268 HCAPLUS  
DOCUMENT NUMBER: 120:236268  
TITLE: Towards defining receptors for L-tyrosine and L-DOPA  
AUTHOR(S): Slominski, Andrzej; Paus, Ralf  
CORPORATE SOURCE: Dep. Pathol., Albany Med. Coll., Albany, NY, 12208, USA  
SOURCE: Mol. Cell. Endocrinol. (1994), 99(2), C7-C11  
CODEN: MCEND6; ISSN: 0303-7207  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review, with 69 refs. The authors postulate that in mammalian systems neurotransmitter and hormone-like functions of L-tyrosine (LT) and DOPA (LD) are mediated via specific membrane-bound and/or **nuclear receptors**. The structure and function of these receptors may represent an evolutionary continuum of **regulatory proteins** binding LT or LD in unicellular and lower multicellular organisms.

L6 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:209988 HCAPLUS  
DOCUMENT NUMBER: 120:209988  
TITLE: Convergence of multiple nuclear receptor signaling pathways onto the long terminal repeat of human immunodeficiency virus-1  
AUTHOR(S): Ladas, John A. A.  
CORPORATE SOURCE: Dep. Med., New England Deaconess Hosp., Boston, MA, 02215, USA  
SOURCE: J. Biol. Chem. (1994), 269(8), 5944-51  
CODEN: JBCHA3; ISSN: 0021-9258  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A composite element that interacts with multiple **nuclear receptors** was identified in the long terminal repeat (LTR) of the human immunodeficiency virus-1 (HIV-1). This element, designated **nuclear receptor-responsive element (NRRE)**, spans the -356 to -320 LTR region and contains tightly clustered binding sites for the retinoid X receptor-.alpha. (RXR.alpha.) and for 5 **nuclear receptors** with unknown ligands, apolipoprotein AI **regulatory protein-1 (ARP-1)**, v-erbA-related proteins-2 and -3 (EAR-2 and EAR-3), hepatocyte nuclear factor-4 (HNF-4), and nerve growth factor-inducible protein-B (NGFI-B). The NRRE also interacts with heterodimers formed between RXR.alpha. and either ARP-1, EAR-2, EAR-3, the retinoic acid receptor-.alpha. (RAR.alpha.), or the peroxisome proliferator-activated receptor (PPAR). Remarkably, **nuclear receptor** binding is conserved in the LTRs of recently evolved HIV-1 strains but it is absent in the oldest and most divergent viral isolates, raising the intriguing possibility that the NRRE has been evolved recently in the viral genome. Cotransfection expts. in human choriocarcinoma JEG-3 cells have shown that the HIV-1 LTR-driven transcription is activated by RXR.alpha. and RAR.alpha. in the presence of 9-cis- and all-trans-retinoic acid, by PPAR and RXR.alpha. in the presence of clofibric acid and 9-cis-retinoic acid, and by the "orphan" receptors HNF-4 and NGFI-B. These findings suggest that a complex network of **nuclear receptor** signaling pathways, that include 9-cis- and all-trans-retinoic acid, fatty acids, peroxisome proliferators, growth factors, membrane depolarization, and possibly other signals, converge onto the HIV-1 NRRE and may participate in modulation of viral gene expression.

L6 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:98030 HCAPLUS

DOCUMENT NUMBER: 120:98030

TITLE: Steroidogenic factor 1, an orphan nuclear receptor, regulates the expression of the rat aromatase gene in gonadal tissues

AUTHOR(S): Lynch, John P.; Lala, Deepak S.; Peluso, John J.; Luo, Wei; Parker, Keith L.; White, Bruce A.

CORPORATE SOURCE: Health Cent., Univ. Connecticut, Farmington, CT, 27710, USA

SOURCE: Mol. Endocrinol. (1993), 7(6), 776-86

CODEN: MOENEN; ISSN: 0888-8809

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In a concerted anal. of the genes encoding 3 mouse steroid hydroxylases, the authors identified and characterized a transcriptional **regulatory protein**, designated steroidogenic factor 1 (SF-1), that contributes to the coordinate expression in adrenocortical cells. SF-1, an orphan member of the **nuclear receptor** family, binds to PyCAAGGPyCPu motifs upstream of the steroid hydroxylase genes to regulate their expression. In the present study, the authors extend these findings by examg. the role of SF-1 in regulation of the rat P 450 aromatase gene in gonadal tissues. The 5'-flanking region of the rat aromatase gene was isolated by a PCR-based approach, using primers corresponding to the 5'- and 3'-ends of a published aromatase sequence. DNA sequence anal. revealed 3 differences between the authors' sequence and the previously published sequence, including a 44-base pair (bp) insertion. Moreover, the transcription initiation site, as detd. by primer extension anal., differed from that previously proposed. The new transcription initiation site is located 23 bp 3' of a putative TATA box. When a revised rat sequence was compared to that of the human aromatase PII promoter by BESTFIT anal., a region of .apprx.3000 bp was identified that was 80% conserved between the 2 promoters. A potential SF-1 site, CCAAGGTCA, was identified at position -82 within this region. An oligonucleotide probe contg. this putative SF-1 site was used in gel mobility shift assays. Consistent with previous studies, a specific complex was obsd. with nuclear exts. from gonadal steroidogenic tissues but was absent with nuclear exts. from nonsteroidogenic tissues. The role of SF-1 in this steroidogenic cell-specific complex was next addressed

more directly. Bacterial exts. contg. an SF-1 glutathione S-transferase fusion protein interacted specifically with the putative SF-1 site, and polyclonal antisera against SF-1-glutathione S-transferase specifically abolished the complex formed with nuclear exts. from rat ovaries or R2C rat Leydig tumor cells. Finally, the aromatase SF-1 element increased expression of an SV40 promoter/luciferase construct in transient transfection expts. in a steroidogenic cell-selective manner. Collectively, these studies implicate SF-1 in the regulation of steroid hydroxylase gene expression in nonadrenal tissues, significantly extending previous studies in adrenocortical cells.

L6 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:424492 HCAPLUS

DOCUMENT NUMBER: 115:24492

TITLE: Homology of the ligand-binding regions of Rhizobium symbiotic **regulatory protein** NodD and vertebrate **nuclear receptors**

AUTHOR(S): Gyorgypal, Zoltan; Kondorosi, Adam

CORPORATE SOURCE: Inst. Genet., Hung. Acad. Sci., Szeged, H-6701, Hung.

SOURCE: Mol. Gen. Genet. (1991), 226(1-2), 337-40

CODEN: MGGEAE; ISSN: 0026-8925

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review and discussion, with .apprx.30 refs., on gene modD protein of Rhizobium bacteria and nuclear receptors of vertebrates including (1) signal compds., (2) ligand-binding domains, and (3) mol. evolution.

L6 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1972:524334 HCAPLUS

DOCUMENT NUMBER: 77:124334

TITLE: Nuclear DHT [5.alpha.-dihydrotestosterone] -receptor in Tfm/Y kidney cell

AUTHOR(S): Drews, Ulrich; Itakura, Hideyo; Dofuku, Ryuichi;

Tettenborn, Ulrich; Ohno, Susumu

CORPORATE SOURCE: Dep. Biol., City of Hope Med. Cent., Duarte, Calif., USA

SOURCE: Nature (London), New Biol. (1972), 238(85), 216-17

CODEN: NNBYA7

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The concept of whether the cytosol and nuclear DHT-receptor protein underwent a true mutational change in Tfm/Y kidney cell of the mouse was examd. The elution profile of Tfm/Y nuclear ext. showed 2 proteinbound peaks. The void vol. peak may be DHT-bound **nuclear receptor** protein aggregated to addnl. components. A 2nd peak, mol. wt. of 220,000 may represent the tetrameric form of DHT-bound **nuclear receptor** protein. High affinity cytosol receptor protein which enters the nucleus when bound to DHT is not a **regulatory protein** specified by the Tfm locus.